REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Summary of Telephone Interview

Applicants wish to thank the Examiner and her Supervisor for discussing the above-identified application with Applicants' representative on November 10, 2010.

During the interview, Applicants' representative asserted that Applicants have provided the evidence requested by the Examiner, because the WO 99/34832 reference mentioned in the specification actually corresponds to the cited Onodera reference. The Examiner indicated that she was aware of this correspondence. However, the Examiner requested clarification regarding the ingredients included in the examples of Applicants' specification. The Examiner also requested evidence regarding other surfactants, such as HPMC.

Applicants' representative discussed the distinctions between inhibiting crystallization in non-fat versus fat materials. The Examiner indicated that such comments may be helpful in advancing prosecution, and she requested that these remarks be included in the response.

Lastly, the Examiner suggested amending claim 1 to incorporate a time period for retaining amorphous cefditoren. In the Interview Summary dated November 17, 2010, the Examiner stated that Applicants' own results demonstrate a maximum of three days. However, Applicants note that Examples 8-13 also retain amorphous for more than two days.

Applicants have incorporated the Examiner's helpful suggestions into the response, as discussed below.

Claim Amendments

Claim 1 has been amended to recite that the crystallization of the amorphous cefditoren pivoxil is inhibited in aqueous medium for a period of at least two days. Claim 34 has been cancelled without prejudice or disclaimer.

Information Disclosure Statement

The Examiner is respectfully requested to consider the Information Disclosure Statement, filed concurrently herewith.

Rejection Under 35 U.S.C. § 103(a)

Claims 1-19, 32, 34, and 39-41 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Onodera et al. (US 6,486,149) in view of Nakamura (Foods and Food Ingredient Journal of Japan, 1999, Vol. 180, pp. 2). This rejection is respectfully traversed.

The Examiner relies on Onodera et al. as teaching a process of making amorphous cefditoren pivoxil with a water soluble high molecular additive. The Examiner acknowledges that Onodera et al. fail to teach the addition of sucrose fatty acid ester (SE) into the composition, and fail to teach the weight ratios of SE to cefditoren pivoxil, as required by Applicants' claims. The Examiner contends that the differences are obvious to those skilled in the art in light of the Nakamura reference (FFI Journal No. 180 (1999)).

Specifically, the Examiner states on page 5 of the Office Action that "one of ordinary skill in the art would have found it obvious to add sucrose fatty acid ester to the composition of Onodera since Nakamura teaches that sucrose fatty acid ester (SE) is able to inhibit the formation of crystals in compositions."

Further, the Examiner asserts that it is incumbent upon Applicants to demonstrate through side by side comparative results that the composition of Onodera does not maintain its amorphous character.

Applicants respectfully disagree with the Examiner's positions.

Initially, Applicants respectfully assert that **it would not have been obvious** to add sucrose fatty acid ester to the composition of Onodera, based on the teachings of Nakamura. In the previously filed response, Applicants presented arguments that Nakamura fails to suggest the use of SE for inhibiting the crystallization of an amorphous material. On page 2 of the outstanding Office Action, the Examiner states that "the disclosure of Nakamura et al. would have suggested to one of ordinary skill in the art to try SE for crystal inhibition irrespective of the type of material." However, Applicants disagree with this general assertion.

The Nakamura reference belongs to a **different technical field** than that of the present invention, and therefore fails to teach or suggest the use of SE for inhibiting crystallization of an amorphous material, such as amorphous cefditoren pivoxil. In other words, one of ordinary skill in the art would not have looked to the teachings of the Nakamura reference in order to modify the teachings of Onodera to arrive at the present invention.

In support of this assertion, Applicants emphasize that (1) the mechanism to inhibit fat crystallization by using SE is completely different from that to inhibit crystallization of a non-fat material, and (2) the inhibition of fat crystallization is achieved by solving SE into fats, not by simply mixing them. More detailed comments in this regard are provided below.

(1) Mechanism to inhibit crystallization

The mechanism to inhibit fat crystallization by using SE is completely different from that to inhibit crystallization of a non-fat material. This is clearly described in Japanese Patent Laid-Open Publication No. 92780/1999 (cited in the Information Disclosure Statement submitted herewith). In particular, please see the English translation of paragraph [0006] of the publication.

When SE is solved in cocoa butter, a glycerin moiety of cocoa butter is incorporated in a glycosylpyranose group of SE. Specifically, SE functions as a template for fat crystallization, so that the fat crystal has a specific crystal form. This phenomenon is called "templating effect." Due to this effect, the fat crystal has a single type of crystal form, and crystallization transfer of cocoa butter is inhibited.

A non-fat material such as cefditoren pivoxil does not have a glycerin moiety in the molecule. Therefore, those skilled in the art would not have expected the teachings of the Nakamura reference to be applicable to non-fat materials, such as amorphous cefditoren pivoxil. In other words, those skilled in the art would not have expected that the crystallization of amorphous cefditoren pivoxil would be inhibited by adding SE to amorphous cefditoren pivoxil.

(2) How to inhibit crystallization

Inhibition of fat crystallization is achieved by solving SE into cocoa butter at a molecular level. This is also described in Japanese Patent Laid-Open Publication No. 92780/1999. Please see the English translation of paragraphs [0012] to [0015] of the publication. The working examples of the '780 publication show that fat crystallization is inhibited by dissolving SE into

cocoa butter.

Neither the '780 publication nor the Nakamura reference teach or suggest that fat crystallization is inhibited by simply mixing SE and cocoa butter. Therefore, those skilled in the art would not have expected that the crystallization of amorphous cefditoren pivoxil is inhibited by adding SE to amorphous cefditoren pivoxil.

Thus, Applicants respectfully assert that the Nakamura reference fails to suggest the use of SE for inhibiting crystallization of a non-fat material, such as cefditoren pivoxil, by simply mixing SE with the non-fat material. In other words, the disclosure of the Nakamura reference is not applicable to the present invention.

On page 4 of the Office Acton, the Examiner states that "Herrera et al. demonstrated that addition of various concentrations of sucrose ester delayed crystallization and this effect occurred over a period of at least 2 days and can vary with cooling rate." The Examiner concludes on the same page that "the unexpected results purported by applicant are neither unobvious nor unexpected since such results are known in the prior art."

However, as discussed above, the mechanism to inhibit **fat crystallization** by using SE is completely different from that to inhibit crystallization of a **non-fat material**, such as cefditoren pivoxil. Therefore, even if the Herrera et al. reference is considered, those skilled in the art would not have expected that the crystallization of amorphous cefditoren pivoxil is inhibited by adding SE to amorphous cefditoren pivoxil.

On page 8 of the Office Action, the Examiner states that "it is incumbent upon applicant to demonstrate through side by side comparative results that the composition of Onodera (not any prior art) does not maintain its amorphous character."

However, Applicants respectfully assert that a direct comparison with Onodera is not required.

The Onodera reference discloses how to prepare an amorphous cefditoren pivoxil material. Specifically, the Onodera reference discloses that a **co-precipitated** amorphous cefditoren pivoxil material can be obtained by dissolving crystalline cefditoren pivoxil and a water soluble high-molecular weight additive, and then co-precipitating the dissolved solution. In the co-precipitated material, amorphous cefditoren pivoxil is **homogeneously** mixed with the water-soluble additive. Thus, it can be said that amorphous cefditoren pivoxil in the co-

precipitated material is mixed with the water soluble additive **at a molecular level**. However, the Onodera reference fails to disclose a **simple mixture** of amorphous cefditoren pivoxil with the water soluble additive.

On the other hand, the claimed pharmaceutical composition relates to **a simple mixture** of amorphous cefditoren pivoxil with sucrose fatty acid ester. (Please see paragraphs [0013] and [0014] of the specification.) The claimed composition can be obtained by simply mixing amorphous cefditoren pivoxil with SE.

Thus, Applicants' compositions are completely different from the compositions of Onodera in the mixture state, i.e., Applicants' compositions are simple mixtures, while the composition of Onodera is a homogeneous mixture. In view of this distinction, Applicants respectfully assert that a direct comparison between the present invention and Onodera is unnecessary, as such a comparison would involve variables other than the distinction between SE and e.g., HPMC.

Instead, Applicants present evidence that SE does not behave similarly to the "other surfactants" in Onodera, such as HPMC, PVP and HPC. Applicants direct the Examiner's attention to the technical article of Yokoi et al., (International Journal of Pharmaceutics, 290, (2005), pages 91-99). (This reference is cited on the Information Disclosure Statement, submitted herewith.) [Applicants note that one of the inventors of the present application is an author of this article.]

Specifically, Table 1 of the article shows that 1% SE performs in an unexpected and superior manner in comparison with 1% HPMC. Specifically, 1% SE prolonged the amorphous-maintaining time to 5 days, while 1% HPMC maintained amorphousness for only 3 days.

Table 2 of the article demonstrates that SE has much higher surfactant activity in comparison with HPMC. In fact, Table 2 shows that HPMC has almost no surfactant activity.

Figure 10 of the article shows the structural difference between SE and HPMC, and that the degree of structural hindrance in HPMC would be greater than that in SE. Figure 10 and the description thereof suggest that SE would adsorb onto the interaction sites, which HPMC could not absorb due to its size. This also applies to other polymers, such as HPC and PVP disclosed in Onodera.

Accordingly, Applicants have demonstrate that SE has unexpected and superior results,

when compared to the "other surfactants" of the Onodera reference.

In summary, the Examiner acknowledges that Onodera does not teach the incorporation of SE into the compositions. The Examiner asserts that Nakamura suggest incorporating SE into the compositions of Onodera. However, as discussed above, one of ordinary skill in the art would not have been motivated to look to the teachings of Nakamura, which relate to a completely different technical field, in order to alter the teachings of Onodera and arrive at Applicants' invention.

Further, during the telephonic interview, the Examiner requested evidence that SE has unexpected and superior results, compared to HPMC. Applicants have provided such evidence.

In view of the arguments provided above, Applicants respectfully assert that the subject matter of the present claims is patentable over the cited references. Withdrawal of the rejection is respectfully requested.

Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that the ground of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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